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Use of vitamin D supplements during infancy in an international feeding trial

Eveliina Lehtonen¹, Anne Ormiston², Anita Nucci³, David Cuthbertson⁴, Susa Sorkio¹, Mila Hyytinen⁵, Kirsi Alahuhta¹, Carol Berseth⁶, Marja Salonen⁵, Shayne Taback⁷, Margaret Franciscus⁸, Teba González-Frutos⁹, Tuuli E Korhonen¹, Margaret L Lawson¹⁰, Dorothy J Becker⁸, Jeffrey P Krischer⁴, Mikael Knip^{11,12,13}, Suvi M Virtanen^{1,14,15,*} and TRIGR Investigators†

¹Nutrition Unit, National Institute for Health and Welfare, Mannerheimintie 164a, FIN00300, Helsinki, Finland:

²Department of Paediatrics, University of Tartu, Tartu, Estonia: ³Division of Nutrition, School of Health Professions, College of Health and Human Sciences, Georgia State University, Atlanta, GA, USA: ⁴Pediatrics Epidemiology Center, University of South Florida, Tampa, FL, USA: ⁵Institute of Clinical Medicine, University of Helsinki, Helsinki, Finland: ⁶Medical Affairs Department, Mead Johnson Nutrition, Evansville, IN, USA:

⁷Departments of Pediatrics and Child Health and Community Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada: ⁸Children's Hospital of Pittsburgh of UPMC, University of Pittsburgh, Department of Endocrinology, Pittsburgh, PA, USA: ⁹Endocrinology, Diabetes and Nutrition Research Group/CIBERDEM, Hospital Universitario de Cruces, Barakaldo, Bizkaia, Spain: ¹⁰Division of Endocrinology and Metabolism, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, Ontario, Canada: ¹¹Children's Hospital, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland: ¹²Folkhälsan Research Center, Helsinki, Finland: ¹³Department of Pediatrics, Tampere University Hospital, Tampere, Finland: ¹⁴School of Health Sciences, University of Tampere, Tampere, Finland: ¹⁵Research Center for Child Health, Tampere University and University Hospital, Tampere, Finland

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Abstract

Objective: To examine the use of vitamin D supplements during infancy among the participants in an international infant feeding trial.

Design: Longitudinal study.

Setting: Information about vitamin D supplementation was collected through a validated FFQ at the age of 2 weeks and monthly between the ages of 1 month and 6 months.

Subjects: Infants (*n* 2159) with a biological family member affected by type 1 diabetes and with increased human leucocyte antigen-conferred susceptibility to type 1 diabetes from twelve European countries, the USA, Canada and Australia.

Results: Daily use of vitamin D supplements was common during the first 6 months of life in Northern and Central Europe (>80% of the infants), with somewhat lower rates observed in Southern Europe (>60%). In Canada, vitamin D supplementation was more common among exclusively breast-fed than other infants (e.g. 71% *v.* 44% at 6 months of age). Less than 2% of infants in the USA and Australia received any vitamin D supplementation. Higher gestational age, older maternal age and longer maternal education were study-wide associated with greater use of vitamin D supplements.

Conclusions: Most of the infants received vitamin D supplements during the first 6 months of life in the European countries, whereas in Canada only half and in the USA and Australia very few were given supplementation.

Keywords
Vitamin D
Supplementation
Infancy

Some developed countries^(1–4) have reported a resurgence of vitamin D deficiency and rickets in children and infants, in spite of national recommendations for vitamin D supplementation in infancy. The content of vitamin D in breast milk is very low^(5,6) and thus exclusively breast-fed

children have greater risk of developing vitamin D deficiency than children receiving infant formula⁽⁷⁾. Adequacy of prenatal vitamin D transfer depends on maternal vitamin D stores, which have been shown to be inadequate in many countries⁽⁸⁾. Natural food sources of vitamin D are few, the most common being egg yolk and fish⁽⁹⁾. Vitamin D fortification of foods has become

† See Appendix for a full list of the TRIGR Investigators.

common in various countries. Typical fortified food items are milk, margarine, juices and breakfast cereals⁽¹⁰⁾. Also, infant formulas are fortified with vitamin D. Recommendations given for the use of vitamin D supplements during infancy are currently quite uniform in different countries^(11–13), while compliance with these recommendations varies widely^(14–16). There is a lack of internationally comparable data on vitamin D supplement use.

The Trial to Reduce IDDM in the Genetically at Risk (TRIGR; IDDM = insulin-dependent diabetes mellitus) is an international, randomized, double-blinded study testing the hypothesis whether weaning to an extensively hydrolysed infant formula reduces the risk of developing type 1 diabetes (T1D) in children with increased genetic disease susceptibility⁽¹⁷⁾. The TRIGR prospective nutrition questionnaires provide a unique opportunity to compare information on vitamin D supplement use in different countries. Through that study we aimed to determine how vitamin D supplements were used in infancy in the TRIGR countries and to assess adherence with national recommendations. Further, we assessed how infant feeding, sociodemographic and perinatal factors, region and maternal T1D were related to the use of vitamin D supplements.

Experimental methods

Study population

Newborn infants with a biological first-degree relative affected by T1D as defined by the WHO were invited into the study. The families were recruited when the mother was in late pregnancy (gestational age 35 weeks or more) or immediately after the delivery. Human leucocyte antigen (HLA) genotyping was performed from cord blood or from a blood sample obtained before the age of 8 d. Infants with increased HLA-conferred susceptibility to T1D were eligible to participate in the study. Altogether 2159 infants from twelve countries in Europe and from the USA, Canada and Australia, born between May 2002 and February 2007, were included in the TRIGR study. Of these, 1095 were born to women with diabetes and 1064 to unaffected women. The TRIGR countries have been divided into seven regions: Northern Europe (Finland and Sweden, *n* 521); Central Europe I (Czech Republic, Estonia, Hungary and Poland, *n* 317; i.e. transition economies); Central Europe II (Germany, Luxembourg, the Netherlands and Switzerland, *n* 184); Southern Europe (Italy and Spain, *n* 114); the USA (*n* 393); Canada (*n* 528); and Australia (*n* 102). The study was conducted according to the guidelines laid down in the Declaration of Helsinki. The ethical committee of each site approved the study and signed consent was obtained from the parents or legal guardians of the infant.

Exclusion criteria included multiple gestation, an older sibling already participating in TRIGR, recognizable

severe illness, gestational age <35 weeks, age of the infant more than 7 d at randomization, or no HLA sample drawn before the age of 8 d. Breast-feeding was encouraged. Infants were randomized to receive either a regular cow's milk-based infant formula or an extensively hydrolysed infant formula (Nutramigen®; Mead Johnson, Evansville, IN, USA) upon weaning from breast milk in the first 6–8 months of life. If mother's own breast milk or banked breast milk was not available before randomization, these infants were given Nutramigen in order to avoid exposure to intact cow's milk proteins. Those infants who had received any infant formula other than Nutramigen prior to randomization were excluded. Finally, families having any other reasons (e.g. religious, cultural, unwillingness) to refuse feeding the infant with cow's milk-based products were excluded. Study formulas were enriched with vitamin D. The study did not interfere with the standard feeding practices of the infants other than the avoidance of non-study formulas and foods containing cow's milk or beef.

Dietary interviews

Information on infant feeding was acquired from the family through standardized dietary interviews. Data on vitamin D supplement use were collected with a validated⁽¹⁸⁾ FFQ at several time points during the first year of life. The content of vitamin D in the supplements was not inquired and therefore the amount of supplemental vitamin D could not be calculated. In the present study, vitamin D supplementation refers to the use of vitamin D as supplements and does not include the intake of vitamin D from infant formulas or other foods. Mothers were interviewed by a study nurse or dietitian by telephone when the child was 2 weeks, 1 month, 2 months, 4 months and 5 months old, and at study centre visits at the ages of 3 and 6 months.

Of randomized families, 99.6% (varied between 98.3 and 100% in the different regions) participated in the first interview (at the age of 2 weeks) and 98.8% (varied between 98.1 and 100% in the different regions) of them answered the question concerning vitamin D supplement use. Of randomized families, 98.8% (varied between 95.6 and 100% in the different regions) participated in the study visit at the age of 6 months and 95.0% (varied between 92.4 and 98.3% in the different regions) of them answered the vitamin D supplement question.

Statistics

The use of vitamin D supplements was divided into two categories: (i) any use and (ii) daily use. The daily use was defined as 4–7 times/week. The use of vitamin D supplements was recorded at each dietary interview. The associations of sociodemographic and perinatal factors with the use of vitamin D supplements at 6 months of age were analysed using univariate and multivariate logistic regression analyses. The results are shown as

odds ratios and 95% confidence intervals. All statistical tests were two-sided, at a significance level of $P < 0.05$, and performed using the SAS statistical software package version 9.1.

Results

Vitamin D supplementation from 2 weeks to 6 months of age varied significantly by region (Table 1). Most of the infants who received vitamin D supplements were given them daily. From 2 weeks up to 6 months of age, more than 80% of the infants received vitamin D supplements in Northern (Finland and Sweden) and Central Europe (Czech Republic, Estonia, Hungary, Poland, Germany, Luxembourg, the Netherlands and Switzerland), over 60% in Southern Europe (Italy and Spain), and approximately 50% in Canada. Less than 2% of infants in the USA and Australia received vitamin D supplements between the age of 2 weeks and 6 months (Table 1).

There were no significant differences in the vitamin D supplementation of infants between mothers with and without T1D (see online supplementary material, Supplemental Table 1). When vitamin D supplement use was examined in relation to exclusive breast-feeding, differences between those exclusively breast-fed up to at least 5 months and the others were notable only for Canada, with exclusively breast-fed infants receiving more supplementation than the other infants (Table 2).

Maternal T1D, caesarean section and living in Central Europe II, Southern Europe and Canada were associated

with less frequent use of vitamin D supplements, whereas higher gestational age was associated with more frequent use of vitamin D supplements at the age of 6 months in univariate analysis (Table 3). When all the factors associated with the use of vitamin D supplementation at 6 months of age were considered simultaneously in a multivariate analysis, higher gestational age, older maternal age and longer maternal education were associated with more frequent use of vitamin D supplements (Table 3). Infants living in Central Europe II, Southern Europe and Canada were less likely to get vitamin D supplementation when compared with those living in Northern Europe. The USA and Australia were not included in the analysis as the use of vitamin D supplements in those regions was very low.

Discussion

In the TRIGR study, the use of vitamin D supplements during the first 6 months of life varied by region with more than 80% of the infants living in Northern and Central Europe receiving supplementation, over 60% in Southern Europe and only half in Canada. The use of vitamin D supplements was extremely rare in the USA and Australia, where very few infants received any supplementation during the first 6 months of life. Higher gestational age and maternal age and longer education were associated with more frequent use of vitamin D supplements. Maternal T1D was not associated with vitamin D supplement use. Considerable difference in supplementation by breast-feeding status was only seen

Table 1 Use of vitamin D supplementation in different regions according to child age: TRIGR (Trial to Reduce IDDM in the Genetically at Risk) study, 2002–2007

Region†	0–2 weeks (%)	2 weeks–1 month (%)	1–2 months (%)	2–3 months (%)	3–4 months (%)	4–5 months (%)	5–6 months (%)
Northern Europe (<i>n</i> 521)							
Any use‡	23.6	84.3	94.2	97.3	97.7	98.1	97.3
Daily use§	2.8	79.7	92.4	94.7	95.0	96.0	96.0
Central Europe I (<i>n</i> 317)							
Any use	46.6	91.6	96.0	97.3	96.3	97.3	97.3
Daily use	22.7	84.4	94.7	95.7	95.7	97.0	95.6
Central Europe II (<i>n</i> 184)							
Any use	52.7	80.8	87.4	87.2	84.4	84.3	82.6
Daily use	41.3	74.7	85.2	83.9	80.0	82.0	79.2
Southern Europe (<i>n</i> 114)							
Any use	30.9	62.3	67.9	68.9	71.8	73.5	77.5
Daily use	23.6	60.4	67.0	67.0	70.9	72.6	75.5
USA (<i>n</i> 393)							
Any use	0.3	0.8	1.0	1.0	1.6	1.6	1.6
Daily use	0.3	0.5	1.0	0.8	1.0	1.0	0.8
Canada (<i>n</i> 528)							
Any use	30.8	49.8	55.0	55.0	53.3	47.7	46.0
Daily use	22.1	42.6	47.5	47.6	45.3	40.5	37.3
Australia (<i>n</i> 102)							
Any use	1.0	0.0	0.0	1.0	0.0	1.0	1.0
Daily use	1.0	0.0	0.0	1.0	0.0	1.0	1.0

IDDM, insulin-dependent diabetes mellitus.

†The following regions were included: Northern Europe (Finland and Sweden); Central Europe I (Czech Republic, Estonia, Hungary and Poland; transition economies); Central Europe II (Germany, Luxembourg, the Netherlands and Switzerland); Southern Europe (Italy and Spain); the USA; Canada; and Australia.

‡Use of vitamin D supplements in any frequency.

§Use of vitamin D supplements 4–7 times/week.

Table 2 Use of vitamin D supplementation in different countries by exclusive breast-feeding status when the child was 5 months old: TRIGR (Trial to Reduce IDDM in the Genetically at Risk) study, 2002–2007

Region	Exclusive breast-feeding	n	0–2 weeks (%)	2 weeks–1 month (%)	1–2 months (%)	2–3 months (%)	3–4 months (%)	4–5 months (%)	5–6 months (%)
Northern Europe	≥5 months	33	24.2	78.8	93.9	97.0	100.0	100.0	100.0
	<5 months	488	23.6	84.6	94.2	97.4	97.6	98.0	97.0
Central Europe I	≥5 months	76	47.4	96.1	100.0	97.3	97.3	98.7	97.3
	<5 months	241	46.4	90.1	94.7	97.3	96.0	96.9	97.3
Central Europe II	≥5 months	33	60.6	81.8	87.9	90.9	90.9	90.9	93.5
	<5 months	151	51.0	87.2	87.2	86.4	83.0	82.8	80.3
Southern Europe	≥5 months	9	11.1	33.3	33.3	44.4	44.4	44.4	55.6
	<5 months	105	32.7	64.9	71.1	71.3	74.5	76.3	79.6
USA	≥5 months	43	0.0	0.0	0.0	0.0	0.0	0.0	2.3
	<5 months	350	0.3	0.9	1.2	1.2	1.7	1.8	1.5
Canada	≥5 months	31	54.8	75.9	71.0	77.4	74.2	67.7	71.0
	<5 months	497	29.2	48.2	54.0	53.5	51.9	46.3	44.4
Australia	≥5 months	17	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	<5 months	85	1.2	0.0	0.0	1.2	0.0	1.2	1.2

IDDM, insulin-dependent diabetes mellitus.

†The following regions were included: Northern Europe (Finland and Sweden); Central Europe I (Czech Republic, Estonia, Hungary and Poland; transition economies); Central Europe II (Germany, Luxembourg, the Netherlands and Switzerland); Southern Europe (Italy and Spain); the USA; Canada; and Australia.

in Canada, where exclusively breast-fed infants received more supplementation.

The present study provides valuable comparative information about vitamin D supplement use in infancy from fifteen countries on three continents. The information on vitamin D supplementation was acquired by an FFQ which was validated against two 48 h recall interviews⁽¹⁸⁾. In the validation study, the agreement of the two methods for vitamin D supplementation was shown to be moderate.

Limitations of the present study are that we did not assess either the dosage of vitamin D supplementation nor vitamin D intake from food. Nor had we an opportunity to measure vitamin D from the peripheral circulation. We were not able to collect data regarding vitamin D supplement use after the age of 6 months. The generalizability of the findings is limited because the study subjects represent a select group of children as they have an increased HLA-conferred susceptibility to T1D as well as a family member affected by T1D. The use of vitamin D supplements may be more frequent in the present risk group since vitamin D intake has been associated with decreased risk of T1D⁽¹⁹⁾.

At the time of the dietary data collection in the TRIGR study (from 2002 to 2007), several of the countries involved in TRIGR had given dietary recommendations for vitamin D supplementation in infants: Sweden and Switzerland recommended a daily supplementation of 10 µg^(20,21); Finland and Estonia from 5 to 10 µg depending on breast-feeding status or amount of infant formula consumed^(22,23); Germany 10 µg⁽²⁴⁾; the Netherlands 5 µg⁽²⁵⁾; and Canada 10 µg until the intake from other sources reached that level⁽¹³⁾. In the USA, vitamin D supplements were previously recommended only for those breast-fed infants not exposed to adequate sunlight and/or whose mothers were vitamin D-deficient⁽²⁶⁾. From 2003 onwards, a daily supplementation of 5 µg was recommended in the USA unless a certain amount of fortified infant formula or milk was consumed⁽²⁷⁾, and in 2008, the recommended dosage for supplementation was doubled to 10 µg⁽²⁸⁾. Also Finland⁽¹²⁾, Estonia⁽²⁹⁾ and the Netherlands⁽²⁵⁾ have increased their recommendation for vitamin D supplementation to 10 µg, and Poland⁽³⁰⁾, Italy⁽³¹⁾ and Spain⁽³²⁾ have given a recommendation of 10 µg daily depending on breast-feeding status or amount of infant formula consumed. In the Czech Republic, the recommended dose for vitamin D supplementation is currently 12.5 µg/d⁽³³⁾ and in Hungary 10 µg⁽³⁴⁾. In Australia, vitamin D supplements are recommended only for specific infant groups with very little sun exposure due to dark skin and/or children with veiled mothers⁽³⁵⁾. With the exception of Australia, the overall recommended amounts of supplementation are now very similar during the first year of life in these countries and also the differences in the recommended age at introduction and end of supplementation are minor. The European Society for

Table 3 Risk for the use of vitamin D supplements according to sociodemographic, perinatal and other background factors at 6 months of age: TRIGR (Trial to Reduce IDDM in the Genetically at Risk) study, 2002–2007

	OR	95 % CI	P value	Adjusted† OR	95 % CI	P value
Age of mother (years)	1.00	0.98, 1.03	0.73	1.04	1.00, 1.08	0.04*
Maternal education (years)	1.03	0.99, 1.07	0.17	1.07	1.00, 1.14	0.04*
Paternal education (years)	1.03	0.99, 1.07	0.17	1.06	1.00, 1.12	0.07
Maternal type 1 diabetes, yes v. no	0.64	0.50, 0.81	<0.001*	1.14	0.78, 1.68	0.50
Gestational age (weeks)	1.21	1.13, 1.31	<0.001*	1.17	1.03, 1.32	0.01*
Male v. female sex of the child	1.05	0.82, 1.33	0.71	0.88	0.64, 1.20	0.42
Caesarean section v. other mode of birth	0.78	0.61, 0.99	0.04*	0.84	0.60, 1.18	0.31
Ponderal index (kg/m ³)	1.01	0.84, 1.22	0.90	0.91	0.72, 1.17	0.47
Region‡						
Northern Europe (reference)	1.00	–	–	1.00	–	–
Central Europe I	1.01	0.41, 2.46	0.99	1.22	0.47, 3.17	0.68
Central Europe II	0.13	0.07, 0.26	<0.001*	0.11	0.05, 0.23	<0.001*
Southern Europe	0.10	0.05, 0.20	<0.001*	0.11	0.05, 0.24	<0.001*
Canada	0.02	0.01, 0.04	<0.001*	0.02	0.01, 0.04	<0.001*

IDDM, insulin-dependent diabetes mellitus.

* $P < 0.05$.

†Adjusted for all the variables in the table.

‡The following regions were included: Northern Europe (Finland and Sweden); Central Europe I (Czech Republic, Estonia, Hungary and Poland; transition economies); Central Europe II (Germany, Luxembourg, the Netherlands and Switzerland); Southern Europe (Italy and Spain); and Canada. The USA and Australia were not included in the analysis as the use of vitamin D supplements in those regions was very low (Tables 1 and 2; online supplementary material, Supplemental Table 1).

Pediatric Endocrinology Bone Club recommends that all breast-fed infants should receive 10 µg of supplemental vitamin D daily from birth until they are receiving the same amount of vitamin D daily from their diet⁽¹¹⁾.

In the current study, the majority of the European children received vitamin D supplements. Almost all the infants (96%) in Northern Europe (Finland and Sweden) were provided vitamin D supplementation daily at the age of 6 months. In an earlier Finnish cohort study, the proportion of children receiving vitamin D supplements was slightly lower: 91% of infants were given supplements at 6 months of age⁽¹⁶⁾. In a large Swedish cohort, 99% of the infants had received vitamin D supplements during the first year of life⁽³⁶⁾. In our survey, 96% of infants were receiving vitamin D supplementation daily at the age of 6 months in Central Europe I countries (transition economies), which include Czech Republic, Estonia, Hungary and Poland. In a previous Polish study, 82% of infants received regular and 14% occasional vitamin D supplementation at the age of 6 months⁽³⁷⁾. In the Central Europe II countries (Germany, Luxembourg, the Netherlands and Switzerland) 79% of the infants were given vitamin D supplements daily at the age of 6 months and 76% of infants in Southern Europe (Italy and Spain). In an earlier Swiss study, only 64% of infants aged 0–9 months had been given vitamin D supplements within the preceding 24 h⁽³⁸⁾. In a Canadian survey the supplementation rate was higher in 2010 than in our study: 80% of infants were supplemented with vitamin D at 2 months of age⁽³⁹⁾. In the USA, a low use of vitamin D supplements during infancy has also been reported in previous studies, being only 4–16% during the first 10 months of life in 2005–2008^(14,15). It is possible that the low rates of supplementation observed in the US TRIGR population are partly due to the fact that the American

Academy of Pediatrics recommendation for vitamin D supplementation was introduced only in 2003, after the TRIGR intervention had started. The lack of vitamin D recommendations for the general population in Australia is reflected in the results of the present study and it is likely that the children participating in TRIGR did not belong to those specific groups for whom supplementation has been recommended.

Even though exclusively breast-fed children have greater risk of developing vitamin D deficiency than children receiving infant formula⁽⁷⁾, it was observed in a recent Canadian report that also those infants consuming both breast milk and infant formula and those consuming only infant formula represented groups at risk of not meeting the recommended 10 µg of vitamin D daily⁽⁴⁰⁾. In a study from the USA it was observed that most (81–98% during the first 10 months of life) exclusively formula-fed infants met the 2003 American Academy of Pediatrics recommendation (5 µg vitamin D/d) that was applicable during the data collection, but only 20–37% would have met the current recommendation of 10 µg/d⁽¹⁴⁾. Among infants fed both breast milk and infant formula, only around one-third met the target of 5 µg/d and less than 15% would have met the current recommendation. In most TRIGR regions, there were no significant differences in vitamin D supplementation between infants exclusively breast-fed for at least 5 months and those who were not. Canada was an exception in this respect; supplement use was more common in the exclusively breast-fed group. Higher frequencies of use compared with the present study but similar difference by breast-feeding status was seen in a report from Canada where 98% of exclusively breast-fed and 88% of infants consuming both breast milk and infant formula had received vitamin D supplementation at some point during the first 6 months

of life in 2008⁽⁴⁰⁾. None of the formula-fed infants had been supplemented with vitamin D. In 2010 in another Canadian study, the supplementation rate of infants receiving only breast milk at 2 months of age was 91% while the corresponding figures for infants receiving both breast milk and infant formula or only infant formula were 79% and 20%, respectively⁽³⁹⁾. Also, in the USA differences in vitamin D supplementation of infants fed only breast milk (5–13% received supplementation), infants consuming both breast milk and infant formula (4–11% received supplementation) and infants consuming only infant formula (1–4% received supplementation) during the first 10 months of life were observed over the time period 2005–2007⁽¹⁴⁾.

Some sociodemographic factors have been associated with the use of vitamin D supplements. Mothers who are younger have been reported to be less likely to give vitamin D supplements to their infants^(16,38); this was also seen in our study. Having more than one child in the family may be associated with less use of vitamin D supplements^(16,38). Higher maternal education was associated with more frequent use of vitamin D supplements in the current study as has been reported before^(40,41).

Vitamin D is particularly important for the skeleton because it is needed for Ca absorption from the intestine. Insufficient vitamin D intake causes rickets in children and osteomalacia in adults. Vitamin D supplementation in infancy has also been associated with reduced risk of T1D⁽¹⁹⁾. There is also some evidence that vitamin D deficiency is associated with increased risk of cardiovascular and autoimmune diseases in adults and lower respiratory infections in children⁽⁴²⁾. The main natural source of vitamin D is the synthesis in the skin induced by UV radiation from the sun⁽⁹⁾. With minimal sun exposure, for example at northern latitudes, or due to protective clothing or sunscreen, other sources of vitamin D are required. Because the intake of vitamin D from food is inadequate for most infants, supplementation is necessary. It is clear that new protocols and strategies are needed in some regions to ensure that families get enough information on the importance of adequate vitamin D intake, especially in infancy and childhood. Re-education about the importance of supplementation is essential as families tend to stop using supplements over time⁽¹⁶⁾.

Conclusion

The importance of adequate vitamin D intake in infancy is well known and supported by the current recommendations for use of vitamin D supplements. In the present study, the recommendations regarding vitamin D supplementation were quite well followed during the first 6 months of life in European countries and to some extent in Canada. The use of vitamin D supplements was conspicuously low in the USA and Australia. Due to

increasing concern regarding the high prevalence of vitamin D deficiency in childhood, and especially in breast-fed infants, action is needed to train health-care personnel and develop strategies to inform families about the importance of adequate intake of vitamin D in infancy, particularly in those exclusively breast-fed.

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Supplementary material

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Appendix

List of TRIGR investigators for publications/version January 2013

Administration/Country	Study centre	Last name	First name	Position
Data Safety Monitoring Board		Mandrup-Poulsen	Thomas	Chair
		Arjas	Elias	Member
		Lernmark	Åke	Member
		Schmidt	Barbara	Member
		Krischer	Jeffrey P.	Observer
International Coordinating Center (ICC), Helsinki, Finland		Åkerblom	Hans K.	PI of the Study until 30.6.08, Deputy PI from 1.7.2008
		Hyytinen	Mila	European Study Monitor
		Knip	Mikael	Deputy PI until 30.6.2008, PI of the Study from 1.7.2008, National Investigator
		Koski	Katriina	European Study Monitor
		Koski	Matti	IT Specialist
		Pajakkala	Eeva	European Study Monitor
		Salonen	Marja	Study Coordinator
Data Management Unit (DMU), Tampa, FL, USA		Cuthbertson	David	Biostatistician
		Krischer	Jeffrey P.	PI of the DMU
		Shanker	Linda	Coordinator
Canadian Coordinating Center, London and Ottawa, ON		Bradley	Brenda	National Coordinator
		Dosch	Hans-Michael	Co-Investigator for Canada
		Dupré	John	Co-PI for North America, National Investigator, Executive Committee
		Fraser	William	Co-Investigator for Canada
		Lawson	Margaret	Executive Committee
		Mahon	Jeffrey L.	Co-Investigator for Canada
		Sermer	Mathew	Executive Committee
		Taback	Shayne P.	Co-Investigator for Canada, Executive Committee
USA Coordinating Center, Pittsburgh, PA and Seattle, WA		Becker	Dorothy	Co-PI for North America, National Investigator, Executive Committee
		Franciscus	Margaret	National Coordinator
		Nucci	Anita	Nutrition Coordinator of North America
		Palmer	Jerry	Executive Committee
Nutritional Epidemiology Unit, Helsinki, Finland		Pekkala	Minna	Research Fellow
		Virtanen	Suvi M.	Head of Nutritional Epidemiology Unit
Australia	AUS01 - Westmead - Children's Hospital	Catteau	Jacki	National Coordinator
	AUS02 - Newcastle - John Hunter Children's Hospital	Howard	Neville	National Investigator
	AUS03 - Sydney - Sydney Children's Hospital	Crock	Patricia	Local Investigator
		Craig	Maria	Local Investigator

Appendix Continued

Administration/Country	Study centre	Last name	First name	Position
Canada	CAN01 - London - St. Joseph's Health Care Centre	Clarson	Cheril L.	Local Investigator
		Bere	Lynda	Co-ordinator
	CAN02 - Vancouver - Children's and Women's Health Centre of British Columbia	Thompson	David	Local Investigator
		Metzger	Daniel	Local Investigator
		Marshall	Colleen	Co-ordinator (In Transition)
	CAN03 - Calgary - Alberta Children's Hospital	Kwan	Jennifer	Co-ordinator (In Transition)
		Stephure	David K.	Local Investigator
		Pacaud	Daniele	Co-Investigator
	CAN04 - Edmonton - Walter MacKenzie Health Sciences	Schwarz	Wendy	Co-ordinator
		Girgis	Rose	Local Investigator
	CAN05 - Winnipeg - Health Sciences Centre	Thompson	Marilyn	Co-ordinator
		Taback	Shayne P.	Local Investigator
	CAN06 - Ottawa - Children's Hospital of Eastern Ontario and The Ottawa Hospital	Catte	Daniel	Co-ordinator
		Lawson	Margaret L.	Local Investigator
		Bradley	Brenda	Co-ordinator
	CAN07 - Toronto Mount Sinai Hospital/Hospital for Sick Children	Daneman	Denis	Local Investigator
		Sermer	Mathew	Co-Investigator
		Martin	Mary-Jean	Co-ordinator
	CAN08 - Quebec - CHUQ	Morin	Valérie	Local Investigator
		Frenette	Lyne	Local Investigator
		Ferland	Suzanne	Co-ordinator
	CAN09 - Saint John – Regional Hospital	Sanderson	Susan	Local Investigator
	CAN10 - Montreal - L' Hôpital Sainte-Justine	Heath	Kathy	Co-ordinator
		Huot	Céline	Local Investigator
		Gonthier	Monique	Co-Investigator
	CAN11 - Montreal Children's Hospital	Thibeault	Maryse	Co-ordinator
		Legault	Laurent	Local Investigator
	CAN12 - Halifax - IWK Health Centre/Dalhousie	Laforte	Diane	Co-ordinator
		Cummings	Elizabeth A.	Local Investigator
	CAN13 - St. John's - Janeway Child Health Center	Scott	Karen	Co-ordinator
		Bridger	Tracey	Local Investigator
	CAN14 - Kingston - Kingston General Hospital/Queen's University	Crummell	Cheryl	Co-ordinator
		Houlden	Robyn	Local Investigator
	CAN15 - Regina - Regina Qu'Appelle	Breen	Adriana	Co-ordinator
		Carson	George	Local Investigator
	CAN16 - Saskatoon - Royal University Hospital	Kelly	Sheila	Co-ordinator
		Sankaran	Koravangattu	Local Investigator
	CAN17 - Peterborough - Peterborough Regional Health Centre	Penner	Marie	Co-ordinator
		White	Richard A.	Local Investigator
Czech Republic	CZE01 - Prague - Faculty Hospital Kralovske Vinohrady	King	Nancy	Co-ordinator
		Popkin	James	Local Investigator
		Robson	Laurie	Co-ordinator
		Al Taji	Eva	National Coordinator
		Aldhoon	Irena	Co-Investigator
		Mendlova	Pavla	National Coordinator
		Vavrinec	Jan	National Investigator
		Vosahlo	Jan	Co-Investigator

Appendix Continued

Administration/Country	Study centre	Last name	First name	Position
	CZE02 - Brno - Hospital Milosrdnych Bratri	Brazdova	Ludmila	Local Investigator
	CZE03 - Olomouc - Faculty Hospital Olomouc	Venhacova	Jitrenka	Local Investigator
		Venhacova	Petra	Co-Investigator
	CZE04 - Usti nad Labem - Hospital of Masryk	Cipra	Adam	Local Investigator
	CZE05 - Ceske Budejovice - Hospital Ceske Budejovice	Tomsikova	Zdenka	Local Investigator
	CZE06 - Plzen - Faculty Hospital Plzen	Krckova	Petra	Local Investigator
	CZE07 - Zlin - Hospital of Bata	Gogelova	Pavla	Local Investigator
Estonia	EST01 - Tallinn - Tallinn Children's Hospital	Einberg	Ülle	Co-Investigator
		Riikjärv	Mall-Anne	Local Investigator
	EST02 - Tartu - Tartu University Children's Hospital	Ormisson	Anne	National Investigator
		Tillmann	Vallo	Co-Investigator
Finland	FIN01 - Helsinki - Hospital for Children and Adolescents, University of Helsinki	Kleemola	Päivi	National Coordinator
		Parkkola	Anna	Local Investigator
		Suomalainen	Heli	National Coordinator
	FIN02 - Helsinki - Department of Obstetrics and Gynecology, University of Helsinki	Järvenpää	Anna-Liisa	Local Investigator
	FIN03 - Espoo - Jorvi Hospital	Hämäläinen	Anu-Maaria	Local Investigator
	FIN04 - Kotka - Kymenlaakso Central Hospital	Haavisto	Hannu	Local Investigator
		Tenhola	Sirpa	Local Investigator
	FIN05 - Lahti - Pajjat-Hame Central Hospital	Lautala	Pentti	Local Investigator
		Salonen	Pia	Local Investigator
	FIN06 - Tampere - Department of Pediatrics, Tampere University Hospital	Aspholm	Susanna	Local Investigator
		Siljander	Heli	Co-Investigator
	FIN07 - Pori - Satakunta Central Hospital	Holm	Carita	Local Investigator
		Ylitalo	Samuli	Co-Investigator
	FIN08 - Jyväskylä - Central Finland Central Hospital	Lounamaa	Raisa	Co-Investigator
		Nuuja	Anja	Local Investigator
	FIN09 - Seinäjoki - South Ostrobothnia Central Hospital	Talvitie	Timo	Local Investigator
Germany	FIN10 - Hyvinkää - Hyvinkää Hospital	Lindström	Kaija	Local Investigator
	FIN11 - Kuopio - Department of Pediatrics, Kuopio University Hospital	Huopio	Hanna	Local Investigator
		Pesola	Jouni	Co-Investigator
	FIN12 - Oulu - Department of Pediatrics, Oulu University Hospital	Veijola	Riitta	Local Investigator
		Tapanainen	Päivi	Co-Investigator
	FIN13 - Hämeenlinna - Kanta-Hame Central Hospital	Alar	Abram	Local Investigator
		Korpela	Paavo	Local Investigator
	FIN14 - Vaasa - Vaasa Central Hospital	Käär	Marja-Liisa	Local Investigator
		Mustila	Taina	Local Investigator
		Virrnsalo	Ritva	Local Investigator
	FIN15 - Lappeenranta - South Carelian Central Hospital			
	FIN16 - Mikkeli - Mikkeli Central Hospital	Nykänen	Päivi	Local Investigator
	GER01 - Hannover - Kinder- und Jugendkrankenhaus – Auf der Bult	Aschemeier	Bärbel	National Coordinator
		Danne	Thomas	National Investigator
		Kordonouri	Olga	Co-Investigator
Hungary	HUN01 - Budapest - Semmelweis Medical University	Krikovszky	Dóra	Co-Investigator
		Madácsy	László	National Investigator

Appendix *Continued*

Administration/Country	Study centre	Last name	First name	Position
Italy	ITA01 - Rome - University Campus Bio-Medico of Rome	Khazrai	Yeganeh Manon	Local Coordinator
		Maddaloni	Ernesto	Local Coordinator
		Pozzilli	Paolo	National Investigator
		Mannu	Carla	Local Coordinator
		Songini	Marco	National Investigator
Luxembourg	LUX01 - Luxembourg - Centre Hospitalier de Luxembourg	de Beaufort	Carine	National Investigator
		Schierloh	Ulrike	Co-Investigator
The Netherlands	NET01 - Rotterdam - Sophia Children's Hospital	Bruining	Jan	National Investigator
		Bisschoff	Margriet	National Coordinator
Poland	POL01 - Wroclaw - Medical University of Wroclaw	Basiak	Aleksander	Co-Investigator
		Wasikowa	Renata	National Investigator
	POL02 - Krakow - Polish-American Children's Hospital	Ciechanowska	Marta	Local Investigator
	POL03 - Katowice - Medical University of Silesia	Deja	Grazyna	Co-Investigator
		Jarosz-Chobot	Przemyslaw	Local Investigator
	POL04 - Lodz - Medical University of Lodz	Szadkowska	Agnieszka	Local Investigator
	POL05 - Lodz - Polish Mother's Memorial Hospital (I.C.Z.M.P.)	Cypryk	Katarzyna	Local Investigator
		Zawodniak-Szalapska	Malgorzata	Co-Investigator
Spain	SPA01 - Hospital de Cruces, University of Basque Country, CIBERDEM-CIBERER, Baracaldo, Bizkaia	Castano	Luis	National Investigator
		Gonzalez Frutos	Teba	Local Coordinator
		Oyarzabal	Mirentxu	Co-Investigator
	SPA02 - Madrid - Hospital Clinico San Carlos	Serrano-Ríos	Manuel	National Investigator
		Martínez-Larrad	María Teresa	Local Coordinator
	SPA03 - Madrid - Hospital Gregorio Marañón	Hawkins	Federico Gustavo	Co-Investigator
		Rodríguez Arnau	Dolores	Co-Investigator
Sweden	SWE01 - Linköping - University of Linköping	Ludvigsson	Johnny	National Investigator
	SWE02 - Uddevalla - Uddevalla Hospital	Smolinska Konefal	Malgorzata	National Coordinator
		Hanas	Ragnar	Local Investigator
	SWE03 - Göteborg - Gothenburg - The Queen Silvia Children's Hospital	Lindblad	Bengt	Local Investigator
	SWE05 - Halmstad - Halmstad Hospital	Nilsson	Nils-Osten	Local Investigator
	SWE06 - Trollhättan - Trollhättan Hospital	Fors	Hans	Local Investigator
	SWE07 - Norrköping - Vrinnevi Hospital	Nordwall	Maria	Local Investigator
	SWE08 - Borås - Borås Hospital	Lindh	Agne	Local Investigator
	SWE09 - Karskrona - Karlskrona Hospital	Edenwall	Hans	Local Investigator
	SWE10 - Örebro - University Hospital	Aman	Jan	Local Investigator
	SWE11 - Jönköping - Ryhovs Hospital	Johansson	Calle	Local Investigator
Switzerland	SWT01 - Zürich - University Children's Hospital	Gadient	Margrit	National Coordinator
		Schoenle	Eugen	National Investigator
USA	USA01 - Pittsburgh - Children's Hospital of Pittsburgh	Becker	Dorothy	USA National Investigator / Pittsburgh Local Investigator
		Daftary	Ashi	Co-Investigator
		Franciscus	Margaret	USA Coordinator/Pittsburgh Coordinator
		Gilmour	Carol	Co-Investigator
	USA02 - Seattle - VA Puget Sound Health Care System and University of Washington	Palmer	Jerry	Local Investigator
		Taculad	Rachel	Coordinator
	USA03 - St. Louis - Washington University	Tanner-Blasier	Marilyn	Coordinator
		White	Neil	Local Investigator

Appendix *Continued*

Administration/Country	Study centre	Last name	First name	Position
	USA04 - Los Angeles - Mattel Children's Hospital of UCLA	Devaskar Horowitz Rogers	Uday Heather Lisa	Local Investigator Coordinator/Dietitian Coordinator/Dietitian
	USA05 - Ponce - Ponce School of Medicine	Colon Frazer Torres	Roxana Teresa Jose	Coordinator Co-Investigator Local Investigator
	USA06 - New York - Naomie Berrie Diabetes Center	Goland Greenberg Nelson Schachner Softness	Robin Ellen Maudene Holly Barney	Local Investigator Coordinator Dietitian Co-Investigator Co-Investigator
Laboratories	HLA-typing Laboratory - Turku - Finland	Ilonen	Jorma	Head of HLA-typing Laboratory
	HLA-typing Laboratory - Pittsburgh - PA - USA	Trucco Nichol	Massimo Lynn	Head of HLA-typing Laboratory Chief Technician
	Cow's Milk Antibody Laboratory - Helsinki - Finland	Savilahti	Erkki	Head of Cow's Milk Antibody Laboratory
	Autoantibody Laboratory - Helsinki - Finland	Härkönen Knip	Taina Mikael	Co-Investigator Head of Antibody Laboratory
	T-Cell Laboratory - Helsinki - Finland	Vaarala Luopajarvi	Outi Kristiina	Head of T-Cell Laboratory Co-Investigator
	T-Cell Laboratory - Toronto - ON - Canada	Dosch	Hans-Michael	Head of T-Cell Laboratory